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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
EMCH, GREGORY S	
ART UNIT	**PAPER NUMBER**
1649	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/084,380	CHAIN, DANIEL G.	
	Examiner	Art Unit	
	Gregory S. Emch	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 May 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *14,19,20,25,55,56,72,75,77-80,83-86 and 93-120* is/are pending in the application.

4a) Of the above claim(s) *99-104 and 109-120* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *14,19,20,25,55,56,72,75,77-80,83-86,93-98 and 105-108* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *05/19/08; 10/21/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Response to Amendment

New claims 93-120 have been added as requested in the amendment filed on 19 May 2008. Following the amendment, claims 14, 19, 20, 25, 55, 56, 72, 75, 77-80, 83-86 and 93-120 are pending in the instant application.

Election/Restrictions

Applicant's election with traverse of an antibody which specifically binds to an epitope within residues 1-5 of amyloid β in the reply filed on 20 August 2008 is acknowledged. The traversal is on the ground(s) that it would not be a serious burden for the Examiner to examine all of the presently pending claims. Applicant alleges that the Examiner has searched and examined claims in this application directed to antibodies that specifically bind epitopes that are co-extensive in scope with the new claims that require the antibody species that specifically binds to an epitope within residues 1-5 or 34-40. Applicant alleges that the Examiner has already performed the searches required to examine the two species between which the Examiner now requires an election. Moreover, Applicant alleges that the Examiner has presented no rationale to support the contention that the species are likely to raise different issues under 35 U.S.C. §§ 101 and/or 112, first paragraph. Applicant alleges that since the search and examination has effectively been completed, it cannot be a "serious burden" for the Examiner to search and examine the complete application.

Applicant's arguments have been fully considered and are not found persuasive. Applicant's attention is directed to MPEP 808.02 which states that in order to establish reasons for insisting upon restriction, the Examiner must show by appropriate explanation one of the following: (A) Separate classification thereof; (B) A separate status in the art when they are classifiable together; (C) A different field of search." There is an examination and search burden for these patentably distinct species due to their mutually exclusive characteristics. The species require a different field of search (e.g., searching different classes/subclasses or electronic resources, or employing different search queries); and/or the prior art applicable to one species would not likely be applicable to another species. More specifically, contrary to Applicant's assertion, the instantly claimed epitopes require a new search and consideration; they have not already been searched or considered. Although the newly claimed epitopes may be co-extensive in scope with the generic claims, said species have not been previously searched or considered. As Applicant is most likely aware, claims drawn to a genus (as in the claims examined previously) do not anticipate claims drawn to specific species (as newly claimed in claims 93-120).

The requirement is still deemed proper and is therefore made FINAL.

Claims 99-104 and 109-120 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to nonelected subject matter, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 20 August 2008.

Claims 14, 19, 20, 25, 55, 56, 72, 75, 77-80, 83-86, 93-98 and 105-108 are under examination in the instant office action.

Information Disclosure Statement

Signed and initialed copies of the IDS papers filed on 19 May 2008 and 21 October 2008 are enclosed in this action.

Response to Arguments

Declarations under 37 CFR 1.132

Applicant's arguments filed on 19 May 2008, with respect to the instant claims being entitled to the benefit of the priority date of 09 April 1997 (because the disclosure of the prior-filed provisional application no. 60/041,850 provides adequate support in the in view of 35 U.S.C. 112, first paragraph for the instant invention) have been fully considered and are partially persuasive. This is based on Applicant's arguments, which outline several portions of the specification of the provisional application, which according to Applicant, provide written description for the instant claims (see e.g. pp.22-25 of the Remarks from 19 May 2008). These remarks, in view of the remarks set forth on pp.25-28, i.e. regarding application of the PTO's new Training Materials on the Written Description requirement (most importantly Example 1C), are found persuasive for some of the claims under examination. Thus, in addition to these remarks, the two declarations under 37 CFR 1.132, which were submitted on 19 May 2008,

are sufficient to establish benefit to a priority date of April 9, 1997 for claims 14, 20, 55, 56, 72 and 75.

However, dependent claims 19, 25, 77-80, 83-86, 93-98 and 105-108 are still denied the benefit of a priority date of 09 April 1997 because the provisional fails to provide support for the limitations of: "an artificial antibody" in claims 19, 25, 80, 86, 93 and 105, the antibody being “targeted to a free N-terminus of an amyloid β peptide fragment truncated at position 3, 11 or 17" in claims 77 and 83, and the antibody being “specific for an amyloid β peptide fragment that begins with a pyroglutamate residue at position 3” in claims 78 and 84 and the antibody being “specific for an amyloid β peptide fragment that begins with a pyroglutamate residue at position 11” in claims 79 and 85. Thus, claims 19, 25, 77-80, 83-86, 93-98 and 105-108, which comprise subject matter that has not been disclosed prior to the filing of the instant application, are given a priority date of **February 28, 2002** (the filing date of the instant application).

Therefore, the declarations and arguments are insufficient to overcome the rejection of claims 19 and 25 under 35 U.S.C. 102(b) as being anticipated by Bard et al. (2000), the rejection of claims 19, 25, 77, 80, 83 and 86 under 35 U.S.C. 102(e) as being anticipated by US Patent 6,787,637 to Schenk and the rejection of claims 78, 79, 84, and 85 under 35 U.S.C. 103(a) as being obvious over Schenk (‘637 patent) in view of Saido et al. (1996) and Harigaya et al. (2000) as set forth previously.

Claim Rejections Withdrawn

The rejection of claims 14, 20, 55 and 56 under 35 U.S.C. 102(b) as being anticipated by Bard et al. (2000) is withdrawn for the reasons set forth above.

The rejection of claims 14, 20, 55, 56, 72 and 75 under 35 U.S.C. 102(e) as being anticipated by US Patent 6,787,637 to Schenk is withdrawn for the reasons set forth above.

Claim Rejections - 35 USC § 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

The rejection of claims 14, 19, 20, 25, 55, 56, 72, 75, 77-80, and 83-86 under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps is maintained for reasons of record and as set forth below. Further, newly presented claims 93-98 and 105-108 are also subject to the instant rejection under 35 U.S.C. 112, second paragraph. The omitted steps are: the step of delivery of a free-end specific anti-Aβ antibody to a patient.

In the reply filed 19 May 2008, Applicant asserts that guidance concerning how exogenous antibodies may be administered, e.g., by intravenous administration or by expression of antibody genes in the CNS is taught in the specification at pages 11-13. Applicant asserts that the present application and the provisional application disclose that antibodies contact amyloid-β protein after being secreted into the CSF from neuronal cells or after they cross the blood brain barrier. Thus, Applicant asserts that the application sets forth how

exogenous antibodies may be present *in vivo* and where the contacting step occurs (in the CSF).

Applicant's arguments have been fully considered and are not found persuasive. Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Regardless of whether the specification teaches that administration is an essential step, the claims are indefinite because without an administration step, it is still unclear to the artisan how exogenous antibodies would be present *in vivo*. In other words, it is still unclear how the antibody gets into the patient in order to evoke the claimed method. Additionally, because the delivery of the antibody is missing, the contacting step is indefinite and thus open to interpretation as to where the contacting step occurs. Therefore, the current amendments are still indefinite.

Furthermore, as stated previously, claims 14, 20, 77 and 83 recite the limitation "said subject" in line 6 of each claim. There is insufficient antecedent basis for this limitation in the claims because the claims recite the term "patient" prior to the appearance of the term "subject."

Claim Rejections - 35 USC § 102

The rejection of claims 19 and 25 under 35 U.S.C. 102(b) as being anticipated by Bard et al. (2000) is maintained for reasons of record and as set forth below. Further, newly presented claims 93, 96-98, 105 and 108 are also subject to the instant rejection.

Applicant argues that Bard does not qualify as prior art because the pending claims are entitled to a priority date of April 9, 1997.

Applicant's argument has been fully considered and is not found persuasive. As set forth above, the instant claims are given the priority date of February 28, 2002. As such, the Bard et al. reference still qualifies as 102(b) prior art.

Regarding newly presented claims 93, 96-98, 105 and 108, these are anticipated by the Bard et al. reference because as stated in the office action dated 03 March 2006, Bard et al. teaches the administration of various monoclonal antibodies to transgenic PDAPP mice, and the reduction of amyloid-pathologies as a result of this administration (see Abstract). PDAPP mice are used a model of Alzheimer's disease (AD), as the mice over-express human amyloid precursor protein (APP) leading to the accumulation of amyloid- β plaques in the brains of these mice as they age, consistent with AD pathology. Bard teaches that the antibodies employed for such treatment include the monoclonal antibody 3D6, which specifically binds to residues 1-5 of amyloid β. Moreover, because the monoclonal antibodies were shown to effectively reduce amyloid- β burden in the frontal cortex when administered to PDAPP mice (see p. 917, Figure 1) and initiate both *in vivo* (see p. 917, Figure 2) and *ex vivo* (see p. 918, Table 1) amyloid clearance, they meet the limitations of the method of obtaining an amyloid β-peptide-antibody complex in claims 93 and 96-98. Moreover, Bard concludes that the monoclonal antibodies are capable of crossing the blood-brain-barrier at therapeutically relevant levels and therefore

should be considered for the treatment of Alzheimer's disease as well as other CNS disorders (see p. 919, 1st column). Thus, the Bard et al. reference anticipates the instant claims 105 and 108.

The rejection of claims 19, 25, 77, 80, 83 and 86 under 35 U.S.C. 102(e) as being anticipated by US Patent 6,787,637 is maintained for reasons of record and as set forth below. Further, newly presented claims 93-98 and 105-108 are also subject to the instant rejection.

Applicant argues that Schenk does not qualify as prior art because the pending claims are entitled to a priority date of April 9, 1997.

Applicant's argument has been fully considered but it is not found persuasive. As set forth above, the instant claims are given the priority date of February 28, 2002. As such, the Schenk reference still qualifies as 102(e) prior art.

Regarding newly presented claims 93-98, these are anticipated by the Schenk patent because as stated in the office action dated 03 March 2006, Schenk discloses methods of preventing or treating a disease associated with amyloid deposits of Aβ in the brain of a patient, such as Alzheimer's disease, by administering an antibody that binds to induces a clearing response against the amyloid deposits (column 2, lines 22-25 and lines 53-55). The antibody used in such methods can be humanized or chimeric, monoclonal, or polyclonal (column 2, lines 59-61), and includes fragments such as separate heavy and light chains, Fab', F(ab')2, Fabc, and Fv (column 7, lines 24-29), and may also be bispecific or

bifunctional (column 7, lines 35-39). Schenk teaches that in some methods, the antibody binds to an epitope comprising a free N-terminal residue of Aβ (column 2 lines 45-46). Examples of such antibodies include the monoclonal antibodies 3D6. Therefore, Schenk discloses all the limitations of claims 93-98 and 103-108

Claim Rejections - 35 USC § 103

The rejection of claims 77-80 and 83-86 under 35 U.S.C. 103(a) as being obvious over Schenk ('637 patent) in view of Saido et al. (1996) and Harigaya et al. (2000) is maintained for reasons of record and as set forth below.

Applicant argues that neither Schenk nor Harigaya qualify as prior art because the pending claims are entitled to a priority date of April 9, 1997.

Applicant's argument has been fully considered and is not found persuasive. As set forth above, the instant claims are given the priority date of February 28, 2002. As such, The Schenk and Harigaya references still qualify as prior art references.

Conclusion

No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory

action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gregory S. Emch whose telephone number is (571) 272-8149. The examiner can normally be reached 9:00 am - 5:30 pm EST (M-F).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey J. Stucker can be reached at (571) 272-0911. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.
/G.E./

Gregory S. Emch, Ph.D.
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17 November 2008

/Elizabeth C. Kemmerer/
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